

REMARKS:

Claims 1-20 are currently pending. Claims 1-3 and 10 are amended.

Claim Objections

Claim 4 is objected to because it recites “(c)” instead of “c).” Applicants have amended said objected to term and favorable action is solicited.

Rejections under 35 USC §101

Claims 10-14 are rejected for allegedly being directed to non-statutory subject matter. The Examiner asserts that because Applicants have employed the term “comprising,” that the claims can be interpreted to include a cell naturally comprising the claimed polynucleotide. Applicants respectfully disagree.

For at least the following reasons, Claim 10 is directed to statutory subject matter. Claim 10 recites “at least one **isolated** nucleic acid sequence” (emphasis added). As such, said the rejections under §101 are in error. Nonetheless, while neither agreeing with the Examiner’s reason for nor agreeing with the correctness of the instant rejection, Applicants have amended Claim 10 to further illustrate that said Claim is directed to statutory subject matter. Favorable action is solicited

Claim Rejections 35 USC §112 ¶2

Claims 1-4, 6 and 8-14 are rejected for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention or because the metes and bounds of said Claims are not clear.

It is well settled that the “language of the claims, read in light of the specification” is to be considered when determining whether the Claims are definite. (*Allen Archery Inc. v Browning MFG. Co.*, 819 F.2d 1087, 1092 (Fed. Cir. 1987)). This precept has been incorporated into the MPEP which states that “[t]he meaning of every term used in any of the claims should be apparent from the descriptive portion of the specification with clear disclosure as to its import.” (MPEP §608.01(o). *See also* 37 CFR 1.75 (c) wherein it states in part that “the meaning of the terms in the claims may be ascertainable by reference to the description.”

Moreover, the definiteness of the language employed “must be analyzed - not in a

vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one processing ordinary skill in the pertinent art.” (*In re Angstadt*, 537 F.2d 498, 501 (C.C.P.A. 1976)(quoting *In re Moore*, 439 F.2d 1232,1235 (C.C.P.A. 1971)). The law is abundantly clear that “if the claims, read in the light of the specifications, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more.” (*North Am. Vaccine, Inc. v American Cyanamid Co.*, 7 F.3d 1571, 1579-1580 (Fed. Cir. 1993)).

The Examiner states that the term “shown in” makes Claims 1 and 4 unclear. While neither agreeing with the Examiner’s reason for nor agreeing with the correctness of the instant rejection, Applicants have amended Claims 1 and 4 to facilitate prosecution of the instant application. Favorable action is solicited.

It is also asserted that it is unclear to the Examiner the meaning of the term “biosynthesis.” Accordingly, to aid the Examiner in said interpretation, the term “biosynthesis” has been deleted from Claim 2 and 3. Favorable action is solicited. Further, Claims 2 and 3 have been amended to better establish the metes and bounds of said Claims in accordance with the Examiner’s assertions. Favorable action is solicited.

Claim Rejections 35 USC §112 ¶1

Claims 1-4, 6 and 8-14 are rejected for allegedly failing to meet the written description and enablement requirements of §112.

In regards to all the 112 ¶1 rejections, it must be remembered that to satisfy the written description prong of 35 USC §112 ¶1, the Specification must only describe the invention in sufficient detail so that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). No particular form of disclosure is required, but “the description must clearly allow persons of ordinary skill in the art to recognize that [the patentee] invented what is claimed.” *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989) (citing *In re Wertheim*, 541 F.2d 257, 262 (C.C.P.A. 1976)).

The Claims are written in such a manner that the problems of insufficient numbers of examples as described by the Examiner in the Office Action should not apply. Applicants’

invention is drawn to an isolated nucleic acid sequence which encodes a fusion protein and which is composed of a combination of a nucleic acid sequence encoding a fatty acid or lipid metabolism. The MPEP states that a “[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces” and as such, a single species may be enough to identify the entire genus (*see* MPEP 2163.II.A.3.a.ii.). A recent Federal Circuit case supports the statements of the MPEP. When discussing what is required for a written description the court said “[t]he ‘written description’ requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution” (*Capon v. Eshhar*, 418 F.3d 1349, 1358; (Fed. Cir. 2005)). Further, in overturning a BPAI decision, which relied on similar rejections reasons as stated in the instant Office Action, where both parties to an interference had all Claims in their respective patents cancelled for failing to meet the written description requirement, the court stated that “[t]he Board erred in refusing to consider the state of the art of the scientific knowledge” and when citing *Lilly* and *Fiers* spoke of a rulings in view of a “wish” list provided in said inventions, and not the state of the relevant art (*Id.* at 1357). Further, the court stated, that “[i]t is not necessary that every permutation with a generally operable invention be effective in order for an inventor to obtain a generic claim” and both parties were lauded because they “present[ed] not only general teachings... but also specific examples” (*Id.* at 1359).

Applicants assert that the instant Specification fully complies with these requirements because it allows one of ordinary skill in the art to practice the invention. The claims are written in such a manner that the problems described by the Examiner in the Office Action should not apply. Even the Examiner has stated that Applicants have supplied a polynucleotide encoding a fusion protein comprising a polypeptide of SEQ ID NO: 2 and Δ -4 desaturase which provide exemplifications of the instant invention when not even a single example is required to fulfill the written description requirement. Applicants provide in the instant Specification summary information such as the function of lipids and fatty acids, and general molecular biology techniques which meet the “general teachings” prong. Further, Applicants have supplied “specific examples” of the instant invention as required of the second prong of *Capon*. The instant Specification teaches at least SEQ ID NO: 2 and Δ -4 desaturase. Thus while not required to provide even a single working example (*See, In re Gosteli* above - no specific form of the

disclosure is required), Applicants have provided such specific examples as set forth above and as the Federal Circuit lauded in *Capon*.

Further still, in light of Applicants' amendment changing the percentage homology to 95%, Applicants have provided a claimed genus wherein, contrary to the Examiner's assertions, one of ordinary skill in the art would recognize that Applicants had possession of the instant invention at the time of filing. As noted above, all that is required to meet the written description prong of §112 ¶1 is a description of the invention. Accordingly, the instant Application does provide an adequate written description for one of ordinary skill in the art to practice the instant invention.

Regarding the enablement requirement of §112, the Federal Circuit has held that "[t]he specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation'." (*Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. (2003))). The Claims as currently amended are fully enabled by the Specification of the instant application in combination with the general knowledge of one of ordinary skill in the art.

Further as described in *Capon*, as the skill in the art progresses so does the analysis of the inventions in said art. The Examiner alleges that the instant disclosure presents no guidance or working examples for practicing the instant invention. Applying *Capon* and the relative state of the art at the time of filing, one of ordinary skill would be able to create the working examples the Examiner asserts are lacking and the guidance needed would be minimal, if any was needed at all, as molecular biological techniques are well known to the skilled artisan. The skill in the art at the time of filing was such that creation of polynucleotides, in general, was routine.

Further still, the Examiner makes assertions regarding substituting amino acids, the predictability of results and obtaining the desired activity in the end product. Applicants assert that one of ordinary skill in the art would be able to determine to a sufficient degree, as to not require undue experimentation, amino acid substitutions. First, a skilled artisan would know that in certain positions, certain amino acid changes would render the subsequent protein inactive and would avoid using said substitutions. Along those lines, MPEP 2164.08(b) clearly states that "[t]he presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled." Thus, even if the skilled artisan substituted an amino acid at a non-optimum position, said invention is still enabled. Second, computational techniques were

available at the time of filing for structural predictions based on sequence listings. (*See e.g.*, The Boston University Protein Sequence Analysis server available at <http://bmerc-www.bu.edu/psa/>). Accordingly, one of ordinary skill in the art would have ready knowledge of and predictability of activity after amino acid substitution.

Further yet, the Examiner asserts that to practice the instant invention “would require years of inventive effort.” The Examiner is directed to MPEP 2164.06 wherein *In re Wands* is quoted as stating “[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible” if the experimentation is routine or if the specification provides guidance (858 F.2d 731, 737 (Fed. Cir. 1988)) (citing *In re Angstadt* 537 F.2d 489, 502-04 (CCPA 1976)). Applicants assert 1) that plenty of guidance is provided in the instant Specification in regards to the techniques required to practice the instant invention and 2) that the techniques are routine. As the Examiner surely knows, combinational chemistry is a known skill in the art and the skilled artisan would have been able to use said techniques to screen for active peptides. Accordingly, the instant invention is enabled.

Applicants respectfully submit that for at least the reasons listed above, the rejections under 35 USC §112, first paragraph, written description and enablement, should be withdrawn and an indication of allowance should appear in the next paper from the Office. Favorable action is solicited.

Rejections under 35 USC §103

Claims 1-4, 6 and 8-14 are rejected for allegedly being obvious in light of the art cited by the Examiner in the instant Action. Applicants respectfully disagree.

To establish *prima facie* obviousness, the Examiner must show in the prior art some suggestion or motivation to make the claimed invention, a reasonable expectation for success in doing so, and a teaching or suggestion of each Claim element (*See, e.g., In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ 2d 1941 (Fed. Cir. 1992); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). Most inventions arise from a combination of old elements and each element may often be found in the prior art (*In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998)). However, mere identification in the prior art of each element is insufficient to defeat the patentability of the combined subject matter as a whole (*Id.* at 1355,

1357). Rather, to establish a *prima facie* case of obviousness based on a combination of elements disclosed in the prior art, the Examiner must articulate the basis on which it concludes that it would have been obvious to make the claimed invention (*Id.*). In practice, this requires that the Examiner "explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious" (*Id.* at 1357-59). This entails consideration of both the "scope and content of the prior art" and "level of ordinary skill in the pertinent art" aspects of the *Graham* test.

Moreover, The Examiner appears to have inappropriately bypassed analysis of a number of Applicants' prior arguments by stating that said arguments attacked the references individually. The Examiner is directed to MPEP 2141 wherein it states that,

[i]f the examiner determines there is factual support for rejecting the claimed invention under 35 U.S.C. 103, the examiner must then consider any evidence supporting the patentability of the claimed invention, such as any evidence in the specification or any other evidence submitted by the applicant. The ultimate determination of patentability is based on the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence. *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992).

In this regard, Applicants respectfully reassert all their previous arguments.

The instant invention is drawn related creating fusion proteins between for example fatty acid biosynthesis genes such as a Δ -4 desaturase and the beta-barrel part of the LOX gene. Such fusion proteins are directed to the liposomes or lipid bodies. At said lipid related areas, the fusion protein are integrated into the membranes,

Hohne et al. teaches the biochemical characterization of a lipid body lipoxxygenase from cucumber. Such teachings are disclosed, for example, on the first page, left column, second paragraph with the following, "[w]e first analyzed the properties of fragments from the lipid body lipoxxygenase." The skilled artisan is taught on the second page, left column, that "[l]ipoxxygenase is present in plant cells as many isoforms expressed differently during plant development and located in different tissues and compartments." One of ordinary skill in the art is further taught in the discussion section that "the part of the molecule that may represent a targeting sequence and the domain of this lipoxxygenase form that may be responsible for its attachment to the lipid body surface remain to be determined from the primary structure." Hohne et al. fails to teach or suggest the targeting of fusion proteins between the targeting

sequence and a sequence from the fatty acid biosynthesis chain to liposomes. Thus, said cited art reference fails to teach anything in the technical field of fusion proteins; the reference is related to the physiological characterization of a lipoxygenase from cucumber. Accordingly, there is no teaching or suggestion for the skilled artisan that said targeting sequence can be used in fusion proteins for directing the fusion protein to liposomes. Consequently, one of ordinary skill in the art would not be motivated to combine or modify said cited art, a reference that is in a different technical field and that fails to teach or suggest the fusion proteins of the instant invention, with the expectation of success to practice the said instant invention.

Ohlrogge et al. discloses a polynucleotide encoding a Δ -4 desaturase and its function in the fatty acid biosynthesis chain to synthesis petroselinic acid. Said cited art reference fails to teach or suggest about targeting sequences as such or in combination with other sequences. Further, the reference is absolutely silent about fusion proteins. As with Hohne et al., one of ordinary skill in the art would not be motivated to combine or modify said cited art, a reference that fails to teach or suggest the targeting sequences or fusion proteins of the instant invention, with the expectation of success to practice the said instant invention.

Yamamoto et al. is drawn to a method of producing peptides or proteins which makes it possible to cause a wide range of host microorganisms to produce heterologous fusion proteins and then excise desired gene products efficiently from the fusion proteins using a highly specific enzyme. Said cited art is in the technical field of protein production and protein purification, which is a different technical field. Further, Yamamoto et al. fails to teach or suggest the fusion process for combining LBLOX and desaturase to target lipid bodies. Accordingly, one of ordinary skill in the art would not be motivated to combine or modify said cited art with the expectation of success.

Applicants assert that one of ordinary skill in the art would not have been motivated to combine the above mentioned cited art references. As the courts have noted, a motivation to combine the art cited in a 103 rejection must be present. The Examiner is directed to at least anyone of the following cases - *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential component of an obviousness holding'") (quoting *C.R. Bard, Inc., v. M3 Systems, Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998)); *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the

subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Dance*, 160 F.3d 1339, 1343 (Fed. Cir. 1998) ("there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant"); *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) ("teachings of references can be combined only if there is some suggestion or incentive to do so.") (emphasis in original) (quoting *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577 (Fed. Cir. 1984)).

Moreover, when there is an absence of a motivation to combine, the only possible conclusion is impermissible hindsight reasoning. As the court stated in *In re Fritch*, "[i]t is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teaching of the prior art so that the claimed invention is rendered obvious."

The overall disclosures, teachings, and suggestions of the prior art, and the level of skill in the art - i.e., the understandings and knowledge of persons having ordinary skill in the art at the time of the invention – fail to support the legal conclusion of obviousness. Consequently, a *prima facie* case of obviousness has not been established by the Examiner, and the rejection under 35 USC § 103 should be withdrawn. Favorable action is solicited.